MINNIFIELDS
170344

```
=> fil reg
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  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

=>
=> e papilloma virus/cn 5
E1            1      PAPILIOERYTHRINONE/CN
E2            1      PAPILLAMIDINE/CN
E3            0 --> PAPILLOMA VIRUS/CN
E4            1      PAPILLOSOL/CN
E5            1      PAPILLOSOL DIMETHYL ETHER/CN

=> e human papilloma virus/cn 5
E1            1      HUMAN PANCREATIC SOMATOLIBERIN(1-44) AMIDE/CN
E2            1      HUMAN PANCREATIC SOMATOLIBERIN-40/CN
E3            0 --> HUMAN PAPILLOMA VIRUS/CN
E4            1      HUMAN PARATHORMONE (39-68)/CN
E5            1      HUMAN PARATHORMONE (39-84)/CN

=> e hpv16/cn 5
E1            1      HPU 38/CN
E2            1      HPU 40/CN
E3            0 --> HPV16/CN
E4            1      HPX 209NSL/CN
E5            1      HQ 10125/CN

=> e hpv 16/cn 5
E1            1      HPU 38/CN
E2            1      HPU 40/CN
E3            0 --> HPV 16/CN
E4            1      HPX 209NSL/CN
E5            1      HQ 10125/CN

=> e hpv 18/cn 5
E1            1      HPU 38/CN
E2            1      HPU 40/CN
```

```
E3            0 --> HPV 18/CN
E4            1     HPX 209NSL/CN
E5            1     HQ 10125/CN

=> e protein e6/cn 5
E1            1     PROTEIN E2/NS1 (HEPATITIS C VIRUS KOREAN
STRAIN HCV-K
                    CLONE KC)/CN
E2            1     PROTEIN E3 (EASTERN EQUINE ENCEPHALOMYELITIS
VIRUS STR
                    AIN 82V-2137 CLONE PEE14)/CN
E3            0 --> PROTEIN E6/CN
E4            1     PROTEIN EAAC 1 (RABBIT GLUTAMATE-TRANSPORTING
REDUCED)
                    /CN
E5            1     PROTEIN EAP I (MACACA FASCICULARIS CLONE
PME-EAPI EPID
                    IDYMAL APICAL PRECURSOR REDUCED)/CN

=> e protein e7/cn 5
E1            1     PROTEIN E2/NS1 (HEPATITIS C VIRUS KOREAN
STRAIN HCV-K
                    CLONE KC)/CN
E2            1     PROTEIN E3 (EASTERN EQUINE ENCEPHALOMYELITIS
VIRUS STR
                    AIN 82V-2137 CLONE PEE14)/CN
E3            0 --> PROTEIN E7/CN
E4            1     PROTEIN EAAC 1 (RABBIT GLUTAMATE-TRANSPORTING
REDUCED)
                    /CN
E5            1     PROTEIN EAP I (MACACA FASCICULARIS CLONE
PME-EAPI EPID
                    IDYMAL APICAL PRECURSOR REDUCED)/CN

=> e human mhc class i/cn
E1            1     HUMAN LIVER METALLOTHIONEIN 2 .BETA.-DOMAIN/CN
E2            1     HUMAN MENOPAUSAL GONADOTROPIN/CN
E3            0 --> HUMAN MHC CLASS I/CN
E4            1     HUMAN MOTILIN/CN
E5            1     HUMAN MYELIN BASIC PROTEIN PEPTIDE 69-89/CN
E6            1     HUMAN MYELIN BASIC PROTEIN PEPTIDE 80-89/CN
E7            1     HUMAN N-ACETYL-.BETA.-ENDORPHIN/CN
E8            1     HUMAN NEUROPEPTIDE Y/CN
E9            1     HUMAN NEUROPEPTIDE Y 1-36/CN
E10           1     HUMAN NEUROPEPTIDE Y 13-32/CN
E11           1     HUMAN NEUROPEPTIDE Y 13-36/CN
E12           1     HUMAN NEUROPEPTIDE Y(18-36)/CN

=> e hla a11.2/cn
E1            1     HL402/CN
E2            1     HL548/CN
E3            0 --> HLA A11.2/CN
E4            1     HLA-B60 HISTOCOMPATIBILITY ANTIGEN (HUMAN
ALLELE B*400
```

```
                    12 PRECURSOR)/CN
E5            1     HLB 817/CN
E6            1     HLE/CN
E7            1     HLE1/CN
E8            1     HLE2/CN
E9            1     HLE3/CN
E10           1     HLEI ELASTASE INHIBITOR (HORSE CLONE PHLEI1
LEUCOCYTE)
                    /CN
E11           1     HLEO/CN
E12           1     HLES 100/CN

=> s "hla-a?"/cns
           627 "HLA"/CNS
             0 "A?"/CNS
L1           0 "HLA-A?"/CNS
                 (("HLA"(W)"A?")/CNS)

=> s "hla-a?"/cn
L2           0 "HLA-A?"/CN

=> fil ca
FILE 'CA' ENTERED AT 10:59:37 ON 25 AUG 94
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  HCA File when conducting SmartSELECT searches with large
  numbers of terms.

THIS IS THE BETTER CA FILE.  SEE NEWS FOR DETAILS.

=> s (human papolloma virus or hpv(W)(16 or 18))/ia
        482680 HUMAN/IA
             0 PAPOLLOMA/IA
        141802 VIRUS/IA
             0 HUMAN PAPOLLOMA VIRUS/IA
                 ((HUMAN(W)PAPOLLOMA(W)VIRUS)/IA)
          1111 HPV/IA
        316424 16/IA
        312888 18/IA
           492 HPV(W)(16 OR 18)
L3         492 (HUMAN PAPOLLOMA VIRUS OR HPV(W)(16 OR 18))/IA

=> s (human papilloma virus or hpv(W)(16 or 18))/ia
        482680 HUMAN/IA
          3090 PAPILLOMA/IA
        141802 VIRUS/IA
           592 HUMAN PAPILLOMA VIRUS/IA
                 ((HUMAN(W)PAPILLOMA(W)VIRUS)/IA)
          1111 HPV/IA
```

```
        316424 16/IA
        312888 18/IA
           492 HPV(W)(16 OR 18)
L4         896 (HUMAN PAPILLOMA VIRUS OR HPV(W)(16 OR 18))/IA

=> s (protein(w)(e6 or e7))/ia
DUPLICATE FIELD QUALIFICATION 'HLE'
Terms may be field qualified either individually, e.g.,
'REACTION/TI',
or as a group, e.g., '(REACTION OR SYNTHESIS)/TI'.  However,
both
types of qualification cannot be used at the same time.  For
example,
the expression '(REACTION/CV OR SYNTHESIS)/TI' is not valid.

=> s (protein(w)(e6 or e7))/ia
DUPLICATE FIELD QUALIFICATION 'HLE'
Terms may be field qualified either individually, e.g.,
'REACTION/TI',
or as a group, e.g., '(REACTION OR SYNTHESIS)/TI'.  However,
both
types of qualification cannot be used at the same time.  For
example,
the expression '(REACTION/CV OR SYNTHESIS)/TI' is not valid.

=> s protein/ia(w)(e6 or e7)/ia
DUPLICATE FIELD QUALIFICATION 'HLE'
Terms may be field qualified either individually, e.g.,
'REACTION/TI',
or as a group, e.g., '(REACTION OR SYNTHESIS)/TI'.  However,
both
types of qualification cannot be used at the same time.  For
example,
the expression '(REACTION/CV OR SYNTHESIS)/TI' is not valid.

=> s (protein(w)("e6 or e7"))/ia
        668792 PROTEIN/IA
          1676 "E6"/IA
          1198 "E7"/IA
           337 "E6 OR E7"/IA
                 (("E6"(1W)"E7")/IA)
L5           5 (PROTEIN(W)("E6 OR E7"))/IA

=> s (hpv and human mhc claa i)/ia
          1111 HPV/IA
        482680 HUMAN/IA
          7578 MHC/IA
             4 CLAA/IA
       2253789 I/IA
             0 HUMAN MHC CLAA I/IA
                 ((HUMAN(W)MHC(W)CLAA(W)I)/IA)
L6           0 (HPV AND HUMAN MHC CLAA I)/IA
```

```
=> s (hpv and human mhc class i)/ia
          1111 HPV/IA
        482680 HUMAN/IA
          7578 MHC/IA
        156658 CLASS/IA
       2253789 I/IA
            35 HUMAN MHC CLASS I/IA
                 ((HUMAN(W)MHC(W)CLASS(W)I)/IA)
L7           0 (HPV AND HUMAN MHC CLASS I)/IA

=> s (hpv and hla?)/ia
          1111 HPV/IA
          7850 HLA?/IA
L8          12 (HPV AND HLA?)/IA

=> s l4 and (hla or human mhc or mhc)/ia
          7622 HLA/IA
        482680 HUMAN/IA
          7578 MHC/IA
           188 HUMAN MHC/IA
                 ((HUMAN(W)MHC)/IA)
          7578 MHC/IA
L9          15 L4 AND (HLA OR HUMAN MHC OR MHC)/IA

=> s l9 or l8
L10         20 L9 OR L8

=> d 1-20 an ti so au ai pi ab;d l5 1-5 an .mh

L10  ANSWER 1 OF 20  CA  COPYRIGHT 1994 ACS
AN   121:26884  CA
TI   Peptides of human papilloma virus for
     use in human T cell response-inducing compositions
SO   PCT Int. Appl., 64 pp.
     CODEN: PIXXD2
IN   Kast, Wybe Martin; Melief, Cornelis Joseph Maria; Sette,
Alessandro
     D.; Sidney, John C.
AI   WO 93-NL93  930504
PI   WO 9322338 A1  931111
AB   A peptide comprising an amino acid sequence derived from a
   human papilloma virus (HPV)
     protein, wherein said amino acid sequence has the ability
to bind to
     a human Major Histocompatibility Complex Class I mol., is
claimed.
     The peptides may be used in propylactic or therapeutic
treatment of
     cervical carcinoma and other HPV-related diseases (no
     data).  Nine-residue peptides derived from HPV16 or HPV18
E6 and E7
     proteins which bound to HLA-A2.1, -A1, -A2.1, -A3.2,
     -A11.2, and -A24 mols. were identified.
```

L10 ANSWER 2 OF 20 CA COPYRIGHT 1994 ACS
AN 120:320934 CA
TI Limitations of predictive motifs revealed by cytotoxic T lymphocyte
epitope mapping of the **human papilloma virus** E7 protein
SO Int. Immunol. (1994), 6(2), 289-96
CODEN: INIMEN; ISSN: 0953-8178
AU Sadovnikova, Elena; Zhu, Xiaojiu; Collins, Shona M.; Zhou, Jian;
Vousden, Karen; Crawford, Lionel; Beverley, Peter; Stauss, Hans J.
AB **Human papilloma virus** (HPV) type 16 is found in the majority of cervical cancer patients and the transforming protein E7 is consistently expressed in cancer cells, making it a potential target for immune attack. In this study the authors have investigated whether E7 gains access to the **MHC** class I processing pathway and provides cytotoxic T lymphocyte (CTL) stimulating peptide epitopes. CTL were induced in H-2b mice by immunization with recombinant vaccinia virus expressing E7 (Vac-E7). To map CTL recognition, natural peptides were purified from cells expressing either intact or truncated E7 protein. Following peptide sepn. by HPLC one major CTL epitope was detected and truncated constructs localized this epitope to the C-terminal region. Mapping with synthetic peptides indicated that residues 49-57 (RAHYNIVTF) were recognized by anti-E7 CTL. Synthetic 49-57 peptide was used to induce CTL, which recognized the same HPLC purified natural peptide fractions as anti-E7 CTL. Binding motifs for H-2b class I mols. did not predict residues 49-57 to be a CTL epitope, but instead the sequence 21-28 (DLYCYEQL) which contains a Kb anchor motif. Synthetic 21-28 peptide was found to bind to Kb class I mols. and readily induced CTL, indicating that the T cell repertoire of H-2b mice can recognize this epitope. However, these CTL did not recognize peptides isolated from E7 expressing cells, showing that natural processing did not produce detectable levels of the 21-28

epitope. Together, the data demonstrate that an unexpected E7
peptide can function as a major CTL epitope.

L10 ANSWER 3 OF 20 CA COPYRIGHT 1994 ACS
AN 120:214726 CA
TI Human cytotoxic T lymphocytes stimulated by endogenously processed
human papillomavirus type 11 E7 recognize a peptide containing a
HLA-A2 (A*0201) motif
SO Immunology (1994), 81(2), 222-7
CODEN: IMMUAM; ISSN: 0019-2805
AU Tarpey, I.; Stacey, S.; Hickling, J.; Birley, H. D. L.; Renton, A.;
McIndoe, A.; Davies, D. H.
AB Cytotoxic T lymphocytes (CTL) may play an important role in the
control of human papillomavirus (**HPV**)-induced anogenital
neoplasias, but have been difficult to study owing to the difficulty
in obtg. sufficient quantities of infectious virus. To address this
the authors have stimulated human **HPV**-specific CTL in
vitro using low-d. cells (LDC) from peripheral blood mononuclear
cells (PBMC). Low-d. cells were used to present synthetic peptides,
or endogenously processed peptides expressed from recombinant
vaccinia viruses, to high-d. PBMC (predominantly lymphocytes) for 6
days. Cytotoxic T lymphocytes stimulated with endogenously
processed **HPV** 11 E7 recognized the synthetic **HLA**
-A2 (A*0201) motif-contg. nonamer, 4-12. In reciprocal expts., CTL
stimulated with this peptide in vitro recognized targets expressing
endogenously processed E7. The responses in each case were A2
restricted and peptide specific. Two addnl. A2 motif-contg.
nonamers from **HPV** 6b E7 (21-30 and 47-55) also elicited
peptide-specific, A2-restricted CTL. The data illustrate the
potential that in vitro stimulation with LDC has in understanding
CTL responses to exptl. problematic viral systems such as
HPV, and may offer a route to specific immunotherapy of
HPV-assocd. lesions.

L10 ANSWER 4 OF 20 CA COPYRIGHT 1994 ACS
AN 120:189115 CA
TI Human leukocyte antigen-A2.1 restricted candidate cytotoxic T

lymphocyte epitopes of human papillomavirus type 16 E6 and E7
proteins identified by using the processing-defective human cell
line T2
SO J. Immunother. Emphasis Tumor Immunol. (1993), 14(2), 115-20
CODEN: JIEIEZ; ISSN: 1067-5582
AU Kast, W. Martin; Brandt, Remco M. P.; Drijfhout, J. W.; Melief,
Cornelis J. M.
AB Human papillomavirus type 16 (**HPV-16**) is
strongly assocd. with cervical cancer. **HPV-16**
cytotoxic T lymphocyte (CTL) epitopes may be good candidates for the
development of an antitumor peptide vaccine. A set of 240
overlapping peptides 9 amino acids in length with an 8 amino acid
overlap covering the entire sequence of the 2 viral oncogenes E6 and
E7 was synthesized and tested for its ability to bind to the most
common human leukocyte antigen class I mol. **HLA**-A2.1.
Binding was measured with the human processing defective cell line
T2, which expresses high nos. of empty **HLA**-A2.1 mols. that
are unstable at 37.degree.. These empty mols. can be stabilized by
exogenously added peptides, and the extent of stabilization,
measured by cell surface **HLA**-A2.1-specific staining, can
be taken as a measure of the relative **HLA**-A2.1 binding
affinity. Following this anal., several **HLA**-A2.1 binding
peptides were pinpointed. Preliminary data suggest that at least
one of the high-affinity-binding peptides identified is immunogenic
even in an in vitro priming protocol, underlining the feasibility of
the method described here to identify the immunogenic peptides and
potential candidates for CTL peptide-based vaccines.

L10 ANSWER 5 OF 20 CA COPYRIGHT 1994 ACS
AN 120:160347 CA
TI **HLA** DR-DQ associations with cervical carcinoma show
papillomavirus-type specificity
SO Nat. Genet. (1994), 6(2), 157-62
CODEN: NGENEC; ISSN: 1061-4036
AU Apple, Raymond J.; Erlich, Henry A.; Klitz, William; Manos, M.
Michele; Becker, Thomas M.; Wheeler, Cosette M.
AB Cervical carcinoma is now known to be assocd. with human
papillomaviruses (**HPV**), but the evidence for a link with
specific **HLA** loci is controversial. The role of genetic

variation at the **HLA** class II loci and among **HPV** types in cervical carcinoma was investigated by PCR DNA amplification and oligonucleotide probe type of paraffin-embedded invasive cervical cancer tissue from Hispanic patients and of cervical swabs from Hispanic controls. Certain **HLA** class II haplotypes (such as DRB1*1501-DQB1*602) were assocd. significantly, while DR13 haplotypes were neg. assocd. with cervical carcinoma. These assocns. are HPV16-type specific. These results suggest that specific **HLA** class II haplotypes may influence the immune response to specific **HPV**-encoded epitopes and affect the risk of cervical neoplasia.

L10 ANSWER 6 OF 20 CA COPYRIGHT 1994 ACS
AN 120:132163 CA
TI Expression of immune associated surface antigens of keratinocytes in human papillomavirus-derived lesions
SO Immunobiology (Stuttgart) (1993), 188(4-5), 392-402
CODEN: IMMND4; ISSN: 0171-2985
AU Viac, Jacqueline; Soler, Chantal; Chardonnet, Yvette; Euvrard, Sylvie; Schmitt, Daniel
AB The expression of immune assocd. surface antigens of keratinocytes was studied in human papillomavirus (**HPV**) derived lesions to det. whether **HPV** types have a regulatory role in the pathogenesis of papillomas. A series of cutaneous and mucosal lesions were immunolabeled with monoclonal antibodies to the major histocompatibility complex class I (.beta.2-microglobulin) and II (**HLA**-DR antigens), intercellular adhesion mol. (ICAM-1) and glycoprotein CD36 (OKM5) as well as CD1a (Langerhans cells), CD4, CD8 (T cells) and CD11a (LFA1 antigen). Testing for the presence of **HPV** was carried out by in situ hybridization with biotinylated probes for viral DNA detection and typing. The authors obsd. a drastic redn. or a loss of .beta.2-microglobulin by keratinocytes from cutaneous lesions in correlation with the disappearance of Langerhans cells. Only mild alterations were obsd. in mucosal lesions. **HLA**-DR expressed by keratinocytes was only detected in condylomas and laryngeal papillomas and was usually assocd. with a dense inflammatory reaction. This **HLA**-DR expression may be correlated with an up-regulation of ICAM-1 and the

presence of LFA1 pos. leukocytes, mainly of CD8 phenotype, in the epithelium. CD36 was detected on differentiated keratinocytes of all lesions; its expression seems related to the proliferation state of the lesions and probably does not represent an immune marker. The different reactivity patterns obsd. in cutaneous and mucosal lesions may reflect: 1. different roles for mucosal and cutaneous **HPV** types in the induction of immunoregulatory surface antigens of keratinocytes, or 2. the changing nature of the cytokines released by mononuclear cells and infected keratinocytes in these lesions.

L10 ANSWER 7 OF 20 CA COPYRIGHT 1994 ACS
AN 120:28879 CA
TI **MHC** class I expression in **HPV 16** positive cervical carcinomas is post-transcriptionally controlled and independent from c-myc overexpression
SO Oncogene (1993), 8(11), 2969-75
CODEN: ONCNES; ISSN: 0950-9232
AU Cromme, F. V.; Snijders, P. J. F.; van den Brule, A. J. C.; Kenemans, P.; Meijer, C. J. L. M.; Walboomers, J. M. M.
AB Squamous cell carcinomas of the uterine cervix (n = 23) were selected for the presence of human papillomavirus type 16 (**HPV 16**) using the polymerase chain reaction (PCR). Localization of transcripts coding for the E7 protein was demonstrated in neoplastic cells with RNA in situ hybridization. Consecutive tissue sections were investigated for expression of the major histocompatibility complex class I (**MHC**-I) and c-myc using immunohistochem. double staining procedures, since a role has been suggested for the c-myc protein in **MHC**-I down-regulation and c-myc overexpression has been described in cervical carcinomas. Reduced expression of class I heavy chains was obsd. in neoplastic cells from 18 out of 23 carcinomas (78%). Varying levels of c-myc overexpression were obsd. in 12 carcinomas (52%), from which four showed pos. **MHC**-I expression in c-myc overexpressing cells. In the remaining eight c-myc overexpressing carcinomas **MHC**-I down-regulation was obsd. Addnl. RNA in situ hybridization with class I heavy chain locus-specific RNA-probes revealed presence of class I mRNAs in

those neoplastic cells that show neg. staining for **MHC**-I protein. These data strongly indicate that **MHC**-I down-regulation in cervical carcinomas involves post-transcriptional mechanisms, not directly related to E7 transcription and overexpression of c-myc.

L10 ANSWER 8 OF 20 CA COPYRIGHT 1994 ACS
AN 120:28841 CA
TI Vaccination with cytotoxic T lymphocyte epitope-containing peptide protects against a tumor induced by human papillomavirus type 16-transformed cells
SO Eur. J. Immunol. (1993), 23(9), 2242-9
CODEN: EJIMAF; ISSN: 0014-2980
AU Feltkamp, Mariet C. W.; Smits, Henk L.; Vierboom, Michel P. M.; Minnaar, Rene P.; de Jongh, Barteld M.; Drijfhout, Jan Wouter; ter Schegget, Jan; Melief, Cornelis J. M.; Kast, W. Martin
AB Cytotoxic T lymphocyte (CTL) peptide epitopes can be used for immunization of mice against lethal virus infection. To study whether this approach can be successful against virus-induced tumors the authors generated a B6 (H-2b) tumorigenic cell line transformed by human papillomavirus (HPV). This virus is detected in over 90% of all human cervical cancers. To identify vaccine candidates, the authors generated a set of 240 overlapping peptides derived from the HPV type 16 (HPV16) oncogenes E6 and E7. These peptides were tested for their ability to bind H-2Kb and H-2Db **MHC** class I mols. Binding peptides were compared with the presently known peptide-binding motifs for H-2Kb and H-2Db and the predictive value of these motifs is discussed. The high-affinity H-2Db-binding peptide and putative CTL epitope E7 49-57 (RAHYNIVTF) was used in vaccination studies against **HPV 16**-transformed tumor cells. Immunization with peptide E7 49-57 rendered mice insensitive to a subsequent challenge with **HPV 16** -transformed tumor cells in vivo, and induced a CTL response which lysed the tumor cells in vitro.

L10 ANSWER 9 OF 20 CA COPYRIGHT 1994 ACS
AN 120:6610 CA
TI Relation between skin cancer, humoral responses to human papillomaviruses, and **HLA** class II molecules in renal transplant recipients
SO J. Immunol. (1993), 151(3), 1579-86
CODEN: JOIMA3; ISSN: 0022-1767
AU Bavinck, Jan N. Bouwes; Gissmann, Lutz; Claas, Frans H. J.; Van Der Woude, Fokko J.; Persijn, Guido G.; Ter Schegget, Jan; Vermeer, Bert J.; Jochmus, Ingrid; Mueller, Martin; et al.
AB Human papillomaviruses (**HPV**), esp. the epidermodysplasia verruciformis (EV)-assocd. **HPV** 5, 8, 14, 17, 20, and 47, are thought to play a role in the pathogenesis of some skin cancers in recipients of renal allografts. MHC class I and class II genes are involved in the cellular immune response to viral and tumor antigen (Ag). Little is known about humoral responses to **HPV** in recipients with and without skin cancer. The authors investigated the prevalence of antibodies to the early (E) protein E7 and the major capsid late (L) protein L1 and **HPV** 8. In addn., the authors studied the assocn. of **HLA** class II mols. with these antibody responses. The E7 and L1 open reading frames of **HPV** 8 were bacterially expressed as .beta.-galactosidase fusion proteins, which were purified by preparative gel electrophoresis. Serum samples from 36 renal transplant recipients with and 91 recipients without skin cancer were screened for the presence of IgG and IgM antibodies to **HPV** 8 E7 and L1, by Western blot anal. The detection of anti-**HPV** 8 L1 antibodies represents the immune response to **HPV** 8 and possibly other EV-assocd. **HPV**, because cross-reactivity between the representatives of this **HPV** subgenus can occur. Recipients who had IgM antibodies but no IgG antibodies to L1 of **HPV** 8 (patients with no apparent class switch from IgM to IgG) had skin cancer in 50% of cases, whereas recipients who produced IgG antibodies had skin cancer in only 18% of cases. The estd. relative risk of skin cancer in recipients with no class switch, compared with the risk in those with a good humoral response, was 4.5. The authors found no assocn. between the antibody prodn. in response to L1 of **HPV** 8 and **HLA**

-DR7 was obsd. Renal transplant recipients who have no apparent class switch from IgM to IgG prodn. in response to Ag encoded by L1 of **HPV** 8 or possibly other EV-assocd. **HPV** are at an increased risk of skin cancer. The assocn. with **HLA** -DR7 indicates a genetic control of skin cancer development or regression, involving genes in the class II region of the MHC.

L10 ANSWER 10 OF 20 CA COPYRIGHT 1994 ACS
AN 119:200875 CA
TI Comparative lymphokine secretion by cultured normal human cervical keratinoytes, papillomavirus-immortalized, and carcinoma cell lines
SO Am. J. Pathol. (1993), 142(5), 1544-55
CODEN: AJPAA4; ISSN: 0002-9440
AU Woodworth, Cragi D.; Simpson, Scott
AB The pathogenesis of cervical human papillomavirus (HPV) infection is influenced by the host's immune response. This response depends upon secretion of specific lymphokines to recruit and activate immune cells at the site of infection. To examine whether cervical cells enhance immune-responsiveness, secretion of lymphokines by cultures of normal cervical cells, HPV-immortalized cervical lines, and carcinoma lines was compared. Normal cervical cells constitutively secreted interleukin-1.alpha. (IL-1.alpha.), IL-1.beta., IL-1 receptor antagonist, IL-6, IL-8, tumor necrosis factor-.alpha., and granulocyte macrophage colony stimulating factor. Lymphokines were also produced by exo- and endocervical epithelia in vivo. In contrast, 4 cervical cell lines immortalized by HPV DNAs and 3 carcinoma lines secreted selected lymphokines at significantly reduced levels. Interferon-.gamma. induced major histocompatibility class I and II proteins and intercellular adhesion mol.-I in normal cells, but results in immortal or carcinoma lines were variable. These results suggest that cervical epithelial cells have the potential to influence inflammation and immunity in the cervical mucosa. Furthermore, decreased expression

of lymphokines and histocompatibility mols. by HPV-immortalized cervical cells suggests that similar alterations might accompany persistent HPV infections in vivo.

L10 ANSWER 11 OF 20 CA COPYRIGHT 1994 ACS
AN 118:253247 CA
TI Production and characterization of human proliferative T-cell clones specific for human papillomavirus type 1 E4 protein
SO J. Virol. (1993), 67(5), 2799-806
CODEN: JOVIAM; ISSN: 0022-538X
AU Steele, J. C.; Stankovic, T.; Gallimore, P. H.
AB Human papillomavirus type 1 (**HPV**) virions and E4 protein purified from cutaneous warts were tested in lymphocyte proliferation assays using normal individuals. Both antigens were capable of eliciting good lymphoproliferative responses. Several T-cell clones specific for wart E4 protein were obtained from a donor who had consistently responded very well to E4 in these initial assays. They were maintained in culture by repeated stimulation with antigen and interleukin-2, using an autologous mitomycin-treated lymphoblastoid cell line as a source of antigen-presenting cells. Two of these clones (3F5 and 4A8), which behaved identically, were studied in more detail. A series of overlapping synthetic peptides covering the entire E1-E4 protein sequence was used to identify a single T-cell epitope which maps to a strongly hydrophilic region spanning amino acid residues 38-50. The authors also tested the ability of a panel of major histocompatibility complex class II-matched and -mismatched lymphoblastoid cell lines to present this peptide to the T-cell clones in proliferation assays. The epitope is restricted through **HLA**-DQ7 and it can be recognized by T cells with different T-cell receptor gene rearrangements.

L10 ANSWER 12 OF 20 CA COPYRIGHT 1994 ACS
AN 118:231369 CA
TI **HLA** class I expression and **HPV-16** sequences in premalignant and malignant lesions of the cervix
SO Tissue Antigens (1993), 41(2), 65-71

CODEN: TSANA2; ISSN: 0001-2815
AU Manuel Torres, Luis; Cabrera, Teresa; Concha, Angel; Rosairo Oliva,
Maria; Ruiz-Cabello, Francisco; Garrido, Federico
AB A series of normal cervix epithelia, condylomas, CIN (cervical
intrapithelial neoplasm) I/II (low-grade CIN), CIN III (high-grade
CIN), squamous cell carcinomas, and adenocarcinomas of the cervix
were studied in paraffin-embedded sections for the expression of
MHC class I antigens, using antibodies against **HLA**
antigens and the immunoperoxidase technique. A PCR technique was
also used to evaluate the presence of human papillomavirus (**HPV**)-**16** DNA. All samples from normal tissue,
benign, premalignant, and CIN III lesions expressed **HLA**
class I antigens. However, 15% of the invasive carcinomas
completely lacked **HLA**-B and **HLA**-C antigen
expression, 20% presented a heterogeneous pattern and 2 cases lacked
HLA-B and **HLA**-C heavy chain but retained
.beta.2-microglobulin. **MHC** class I antigen expression on
tumors was compared with clin.-pathol. parameters. The absence of
expression of **HLA** class I mols. was assocd. with the Glanz
histoprognostic index of malignancy. **HPV-16**
sequences were detected in 60% of the condylomas, 88% of the CIN
I/II, 80% of the CIN III, and 82% of the cervical carcinomas.
Eight-six per cent of the tumors expressing **HLA** class I
antigen presented **HPV-16**, whereas only 40% of
the nonexpressing tumors did. Thus, a) **HLA** class I losses
occurred when the tumor became invasive, and in tumors of a more
aggressive histol. type; b) the presence of **HPV-16**
was assocd. with tumors expressing **HLA** class I antigens.

L10 ANSWER 13 OF 20 CA COPYRIGHT 1994 ACS
AN 118:227420 CA
TI Human YB-1 protein binding to enhancer of **human papilloma virus** (**HPV**) type 18
SO Mol. Biol. (Moscow) (1993), 27(1), 81-91
CODEN: MOBIBO; ISSN: 0026-8984
AU Spitkovsky, D. D.; Royer, H. D.; Mazurenko, N. N.; Mikhaleva, I. I.;
Prudchenko, I. A.; Korbukh, I. A.; Sukhova, N. M.; Kisseijov, F. L.
AB Enhancer sequences of **human papilloma virus** (**HPV**) type 18 were used for screening of a
HeLa cell cDNA library in .lambda. gt11 using the protein binding

method. Clones with YB-1 gene homol. sequences were isolated. The
gene codes for a protein which binds the regulatory region of gene Y
for major histocompatibility complex class II (**HLA** 11).
The YB-1 transcripts were found in all samples of cervical
carcinomas. To analyze the protein, rabbit antibodies were produced
to a synthetic peptide, which corresponds to the most hydrophilic
region of the protein. This antipeptide serum permitted
identification of a nuclear 42K protein in HeLa cells as well as in
normal fibroblasts.

L10 ANSWER 14 OF 20 CA COPYRIGHT 1994 ACS
AN 118:37211 CA
TI Induction of cytotoxic T lymphocytes with peptides in vitro:
Identification of candidate T-cell epitopes in **human papilloma virus**
SO Proc. Natl. Acad. Sci. U. S. A. (1992), 89(17), 7871-5
CODEN: PNASA6; ISSN: 0027-8424
AU Strauss, Hans J.; Davies, Huw; Sadovnikova, Elena; Chain, Benny;
Horowitz, Neil; Sinclair, Christine
AB A set of overlapping peptides corresponding to the L1, E6, and E7
proteins of **human papilloma virus** 16
was tested for their ability to bind to major histocompatibility
complex class I mols. and to stimulate cytotoxic T-lymphocyte (CTL)
responses in vitro. A class I binding assay using intact RMA-S
cells showed that 20 of the 99 **human papilloma virus** peptides bound to H-2Kb and/or Db mols. Fifteen of
the 20 class I-binding peptides stimulated primary CTL responses,
whereas peptides that were neg. in the binding assay failed to do
so. Peptide-induced CTLs recognized the immunizing peptide very
efficiently, requiring no more than 1-10 nM peptide for target cell
lysis. However, 2 observations were made that have important
implications for the design of peptide-based vaccines for inducing
CTLs. Not all major histocompatibility complex-binding peptides
that contained known motifs characteristic of naturally processed
peptides induced CTLs. The efficiency of CTL lysis was strongly

decreased when the size of the target peptide differed by only 1
amino acid residue from that of the immunizing peptide. Thus,
peptides chosen for vaccination must correspond in length to
naturally processed peptides.

L10 ANSWER 15 OF 20 CA COPYRIGHT 1994 ACS
AN 117:190111 CA
TI **Human papilloma virus** peptides and
organisms producing said peptides for use in vaccine compositions
SO PCT Int. Appl., 82 pp.
CODEN: PIXXD2
IN Thomas, Elaine Kinney; Chen, Lieping; Blake, James; Hellstrom, Karl
Erik; Hellstrom, Ingegerd; Hu, Shiu Lok
AI WO 91-US7081 910926
PI WO 9205248 A1 920402
AB Immunogenic peptides corresponding to peptides expressed in
mammalian cells in response to **human papilloma virus** (HPV) infection are described. Recombinant organisms
(such as vaccinia virus or tumor cells) producing such a peptide, or
the peptide, can be used to treat HPV infections. Recombinant
vaccinia virus expressing either the HPV E7 or E6 gene, and
mammalian cell expression plasmids contg. these genes, were prepd.
Mice were injected i.p. with HPV E7 epitope-producing fibroblasts,
then challenged by s.c. administration of a tumorigenic dose of M2
melanoma cells transfected with HPV16 E7 expression vector. A
transient development of tumors followed by tumor regression was
obsd.

L10 ANSWER 16 OF 20 CA COPYRIGHT 1994 ACS
AN 117:5669 CA
TI Definition of immunogenic determinants of the human papillomavirus
type 16 nucleoprotein E7
SO Eur. J. Cancer (1992), 28(2-3), 326-33
CODEN: EJCAEL; ISSN: 0959-8049
AU Altmann, Annette; Jochmus-Kudielka, Ingrid; Frank, Rainer;
Gausepohl, Heinrich; Moebius, Ulrich; Gissmann, Lutz; Meuer, Stefan
C.
AB Specific T lymphocyte lines and T cell clones were established from
peripheral blood mononuclear cells of asymptomatic seropos.

individuals employing synthetic peptides which correspond to the sequence of the human papillomavirus (**HPV**) type 16 transforming protein E7. Specificity anal. of T cells as detd. by means of [3H]thymidine incorporation after stimulation with individual peptides revealed 3 immunogenic determinants of E7 that are recognized in assocn. with at least 2 different **HLA** haplotypes. One N-terminal region (amino acids 5-18) was recognized by one T cell line. T cell clones and the corresponding T cell line established from another donor responded to a different N-terminal (17-38) and to a C-terminal region (69-86). The N-terminal sequence 5-18 and the C-terminal determinant contain a periodicity of hydrophilic and hydrophobic residues that have been found in many T cell epitopes. Phenotypic characterization of T cell clones by indirect immunofluorescence revealed that the T cell clones expressed the CD4 surface glycoprotein suggesting that the specific E7 determinants were recognized in assocn. with major histocompatibility complex (MHC) class II mols. With regard to functional properties, at least 3 T cell clones exhibited specific cytotoxic activity towards autologous B lymphocytes transformed by Epstein-Barr virus in the presence of the relevant HPV16 E7 peptides. The implications of these results regarding the development of vaccination strategies and host-virus interaction are discussed.

L10 ANSWER 17 OF 20 CA COPYRIGHT 1994 ACS
AN 116:253852 CA
TI Induction of cytotoxic T lymphocytes specific for a syngeneic tumor expressing the E6 oncoprotein of human papillomavirus type 16
SO J. Immunol. (1992), 148(8), 2617-21
CODEN: JOIMA3; ISSN: 0022-1767
AU Chen, Lieping; Mizuno, Mark T.; Singhal, Mitra C.; Hu, Shiu Lok; Galloway, Denise A.; Hellstrom, Ingegerd; Hellstrom, Karl Erik
AB Human papillomavirus (HPV) type 16 has been implicated in the etiol. of cervical carcinomas, but it is unknown whether HPV-specific

immunity can function in controlling the growth of HPV-assocd. carcinomas. Previously, it was demonstrated that CD8+ T lymphocytes can inhibit the in vivo outgrowth of murine tumor cells transfected with the **HPV-16** E7 gene. Here, a murine model was established to study the cytotoxic T-cell (CTL) responses to the E6 oncoprotein of **HPV-16**. Immunization of C3H/HeN mice with syngeneic fibroblasts expressing a transfected **HPV-16** E6 gene induced regression of transplanted-tumors expressing this gene. Populations of CTL isolated from the spleens of mice whose E6+ tumors had regressed were shown to specifically lyse E6+ target cells. The cytotoxic activity was mediated by CD8+ CTL in a **MHC**-restricted pattern. These data and previous findings with transfected tumor cells expressing the E7 gene, support the conclusion that tumor cells assocd. with **HPV-16** can be inhibited by CTL specific for mols. encoded by the **HPV-16** E6 and E7 genes.

L10 ANSWER 18 OF 20 CA COPYRIGHT 1994 ACS
AN 116:126681 CA
TI Leukoregulin and .gamma.-interferon inhibit human papillomavirus type 16 gene transcription in human papillomavirus-immortalized human cervical cells
SO Cancer Res. (1992), 52(2), 456-63
CODEN: CNREA8; ISSN: 0008-5472
AU Woodworth, Craig D.; Lichti, Ulrike; Simpson, Scott; Evans, Charles H.; DiPaolo, Joseph A.
AB The human papillomavirus (**HPV**) transforming genes E6 and E7 are retained and expressed in the majority of cervical cancers implying an important role for these proteins in maintenance of the malignant phenotype. Leukoregulin (LR) and recombinant .gamma.-interferon (r-IFN.gamma.), lymphokines secreted by immune cells present in regressing **HPV** infections, inhibited transcription of E6/E7 RNAs in several human cervical epithelial cell lines immortalized by recombinant **HPV-16**, -18, and -33 DNAs. R-IFN.alpha. was not effective. Redn. in E6/E7

RNA expression was accompanied by inhibition of cell proliferation
coincident with an increase in epidermal transglutaminase activity,
a marker of squamous differentiation. LR and r-IFN.gamma. enhanced
transcription of class 1 cell surface histocompatibility antigens (
HLA) and r-IFN.gamma. addnl. induced **HLA** class 2
expression. **HPV**-immortalized cells developed partial
resistance to the growth inhibitory effects of lymphokines after
malignant transformation or extended propagation in culture. This
is the first demonstration that LR and r-IFN.gamma. selectivity
inhibit transcription of **HPV**-transforming genes and
suggests a mol. mechanism by which these lymphokines participate in
regression of premalignant cells.

L10 ANSWER 19 OF 20 CA COPYRIGHT 1994 ACS
AN 114:40580 CA
TI Definition of murine T helper cell determinants in the major capsid
protein of human papillomavirus type 16
SO J. Gen. Virol. (1990), 71(11), 2691-8
CODEN: JGVIAY; ISSN: 0022-1317
AU Davies, D. Huw; Hill, C. Mark; Rothbard, Jonathan B.; Chain,
Benjamin M.
AB Three murine major histocompatibility complex (**MHC**) class
II-restricted T cell determinants were identified in the major
capsid protein L1 of human papillomavirus (HPV) type 16. Peptides
derived from **HPV-16** L1, which contain putative T
cell epitopes located by a predictive algorithm, were synthesized
and tested for lymphoproliferative activity by direct immunization,
followed by in vitro assay of responses to peptides or recombinant
HPV-16 L1. The **MHC** restriction of the
stimulatory peptides was detd. using blocking monoclonal antibodies
against class II mols. The responses, which were specific for the
priming peptides alone, cross-reacted with recombinant L1 but not
with analogous peptides derived from other HPV types.

L10 ANSWER 20 OF 20 CA COPYRIGHT 1994 ACS
AN 112:214980 CA

TI Human T cell responses to human papillomavirus type 16 L1 and E6
synthetic peptides: identification of T cell determinants, **HLA**-DR restriction and virus type specificity
SO J. Gen. Virol. (1990), 71(2), 423-31
CODEN: JGVIAY; ISSN: 0022-1317
AU Strang, George; Hickling, Julian K.; McIndoe, G. Angus J.; Howland,
Kevin; Wilkinson, David; Ikeda, Hitoshi; Rothbard, Jonathan B.
AB Four T cell determinants in the major capsid protein of human
papillomavirus (**HPV**) type 16 L1 and one in the E6 protein assocd. with cellular transformation were defined using synthetic
peptides to stimulate peripheral blood mononuclear cells from
asymptomatic individuals. **HLA**-DR restriction was defined using murine L cells transfected with **HLA**-DR genes to present antigen. Responses to two of the five determinants by T
cell lines and clones were shown to be specific for **HPV-16** based on the lack of cross-recognition of the corresponding sequences of other known papillomavirus sequences
(types 1a, 5, 6b, 8, 11, 18, and 33). The T cells raised against
two of the other peptides cross-reacted with corresponding peptides
from other strains to varying extents, depending on their structural
homol. The implications of these results regarding the prevalence
of **HPV-16** infection in the population and the possible diagnostic role of these responses in papillomavirus
infection is discussed.

L5 ANSWER 1 OF 5 CA COPYRIGHT 1994 ACS
AN 121:26884 CA
TI Peptides of human papilloma virus for use in human T cell response-inducing compositions
SO PCT Int. Appl., 64 pp.
CODEN: PIXXD2
IN Kast, Wybe Martin; Melief, Cornelis Joseph Maria; Sette, Alessandro
D.; Sidney, John C.
PI WO 9322338 A1 931111
AI WO 93-NL93 930504
PY 1993
AB A peptide comprising an amino acid sequence derived from a human

papilloma virus (HPV) protein, wherein said amino acid sequence has the ability to bind to a human Major Histocompatibility Complex Class I mol., is claimed. The peptides may be used in propylactic or therapeutic treatment of cervical carcinoma and other HPV-related diseases (no data). Nine-residue peptides derived from HPV16 or HPV18 E6 and E7 proteins which bound to HLA-A2.1, -A1, -A2.1, -A3.2, -A11.2, and -A24 mols. were identified.

L5 ANSWER 2 OF 5 CA COPYRIGHT 1994 ACS
AN 120:213950 CA
TI The predominant mRNA class in HPV16-infected genital neoplasias does not encode the E6 or the E7 protein
SO Int. J. Cancer (1993), 55(5), 791-8
CODEN: IJCNAW; ISSN: 0020-7136
AU Boehm, S.; Wilczynski, S. P.; Pfister, H.; Iftner, T.
PY 1993
AB Human papillomavirus (HPV) type 16 is strongly implicated in the development of progressive neoplasias of the uterine cervix. Its oncogenic potential is decisively detd. by the activity of the early gene products E6 and E7. To look for changes in the expression of these genes during tumor progression the authors cloned subgenomic fragments of HPV16 into RNA expression vectors, which allowed the generation of 35S-labeled riboprobes specific for distinct mRNA classes. Four constructs were made to differentiate between transcripts starting upstream of the E6 ORF or the EI ORF, and one probe was specific for unspliced E6/E7 region transcripts. Five other constructs were used to identify transcripts covering the E1, E2, E4, L1 and L2 regions. With the help of these constructs, the authors analyzed by in situ hybridization 2 low-grade intraepithelial neoplasias of the vulva, 1 high-grade neoplasia of the cervix as well as 4 vulvar and 3 cervical carcinomas. Transcripts from the E1, E2, E4, L1 and L2 region that were consistently detected in the differentiated layers of benign lesions

were variably expressed in precancers and carcinomas. None of the investigated cases revealed detectable amts. of unspliced E6/E7 transcripts with a coding potential for a full-length E6 protein. In benign lesions, the E7 transcripts were confined to isolated nuclei of differentiated cells, whereas high-grade lesions and invasive cancers showed elevated levels of equally distributed E7-specific signals in the cytoplasm of all tumor cells. The most abundant transcripts obsd. in intraepithelial neoplasias and in invasive cancers appear to initiate within ORF E7 and therefore have no coding potential for full-length E6 and E7 proteins. The authors' data show that the actual level of E7-specific transcripts in cancers is lower than anticipated from earlier studies using an ORF E6/E7-specific probe that hybridizes with the 5'-ends of the abundant mRNA class.

L5 ANSWER 3 OF 5 CA COPYRIGHT 1994 ACS
AN 117:86511 CA
TI Targeted degradation of the retinoblastoma protein by human papillomavirus E7-E6 fusion proteins
SO EMBO J. (1992), 11(7), 2425-31
CODEN: EMJODG; ISSN: 0261-4189
AU Scheffner, Martin; Munger, Karl; Huibregtse, Jon M.; Howley, Peter M.
PY 1992
AB The E6 and the E7 proteins of the oncogenic human papillomavirus types 16 and 18 can stably assoc. with p53 and the retinoblastoma protein, resp. The E6-p53 interaction results in the accelerated degrdn. of p53 in vitro via the ubiquitin-dependent proteolysis system. This study demonstrates that a fusion protein consisting of the N-terminal half of the HPV-16 E7 protein and the full length HPV-16 E6 protein promotes the in vitro degrdn. of the retinoblastoma protein. This indicates that the property of the HPV-16 E6 protein to stimulate the degrdn. of p53 can be targeted to

other proteins. Unlike the HPV-16 or HPV-18 E6 protein, the E6 proteins of HPV-6 and 11 do not bind to p53 and consequently do not target p53 for degrdn. Analogous E7-E6 fusion proteins using the E6 proteins of HPV-6 and HPV-11, however, also have the ability to promote the degrdn. of the retinoblastoma protein, indicating that the property to target assocd. proteins for degrdn. is shared by the anogenital specific HPV E6 proteins.

L5 ANSWER 4 OF 5 CA COPYRIGHT 1994 ACS
AN 115:176259 CA
TI Quantitative detection of spliced E6-E7 transcripts of human papillomavirus type 16 in cervical premalignant lesions
SO Virology (1991), 184(2), 795-8
CODEN: VIRLAX; ISSN: 0042-6822
AU Shirasawa, Hiroshi; Tanzawa, Hideki; Matsunaga, Tadashi; Simizu, Bunsiti
PY 1991
AB The splicing patterns of E6-E7 transcripts of human papillomavirus type 16(HPV16) in cervical premalignant lesions were quant. analyzed by S1 nuclease protection assay. The major E6-E7 transcripts in HPV16-contg. cervical lesions (four cervical intraepithelial neoplasias and one invasive carcinoma) were from spliced E6*I/E7 mRNA. The unspliced E6/E7 mRNA, which can encode the full-length zinc finger protein E6, is expressed as 8 to 15% of E6-E7 transcripts. The spliced E6*II/E7 mRNAs were expressed as 14 to 24% of E6-E7 transcripts in most tissues. However, in HPV16-contg. cell lines, the expression levels of spliced and unspliced E6-E7 transcripts were variable.

L5 ANSWER 5 OF 5 CA COPYRIGHT 1994 ACS
AN 110:130788 CA
TI Papillomavirus polypeptides E6 and E7 are zinc-binding proteins
SO J. Virol. (1989), 63(3), 1404-7
CODEN: JOVIAM; ISSN: 0022-538X
AU Barbosa, Miguel S.; Lowy, Douglas R.; Schiller, John T.
PY 1989
AB Papillomavirus proteins E6 and E7 have Cys-X-X-Cys repeats which

have been suggested to mediate zinc binding. A modified assay is developed that detects zinc binding to proteins immobilized on filters. Using well-characterized metalloproteins under reducing conditions, this assay distinguishes proteins that coordinate zinc through cysteine residues from those that bind the metal through other amino acids. Under these conditions, E6 and E7 polypeptides of human papillomavirus type 18 and bovine papillomavirus type 1 exhibited high-affinity zinc binding. The results suggest that E6 and E7 are metalloproteins and may coordinate the metal ions through cysteine residues.

```
=> s (hpv and (cervical(w)(cancer or carcinoma or adenoma)))/ia
          1111 HPV/IA
          8648 CERVICAL/IA
         48006 CANCER/IA
         36565 CARCINOMA/IA
          2936 ADENOMA/IA
           944 CERVICAL(W)(CANCER OR CARCINOMA OR ADENOMA)
L11        267 (HPV AND (CERVICAL(W)(CANCER OR CARCINOMA OR
ADENOMA)))/IA

=> s kast, w?/au;s sette, a??au
L12         78 KAST, W?/AU


'?' TRUNCATION SYMBOL NOT VALID WITHIN 'A??AU'
The truncation symbol ?  may be used only at the end of a search
term.  To specify a variable character within a word use '!',
e.g.,
'wom!n' to search for both 'woman' and 'women'.  Enter "HELP
TRUNCATION" at an arrow prompt (=>) for more information.

=> s sette, a?/au
L13         87 SETTE, A?/AU

=> s sidney, j?/au
L14         17 SIDNEY, J?/AU

=> s l12 and l13 and l14
L15          1 L12 AND L13 AND L14

=> d an .mh

L15  ANSWER 1 OF 1  CA  COPYRIGHT 1994 ACS
```

AN 121:26884 CA
TI Peptides of human papilloma virus for use in human T cell response-inducing compositions
SO PCT Int. Appl., 64 pp.
CODEN: PIXXD2
IN **Kast, Wybe Martin**; Melief, Cornelis Joseph Maria; **Sette, Alessandro D.**; **Sidney, John C.**
PI WO 9322338 A1 931111
AI WO 93-NL93 930504
PY 1993
AB A peptide comprising an amino acid sequence derived from a human papilloma virus (HPV) protein, wherein said amino acid sequence has the ability to bind to a human Major Histocompatibility Complex Class I mol., is claimed. The peptides may be used in propylactic or therapeutic treatment of cervical carcinoma and other HPV-related diseases (no data). Nine-residue peptides derived from HPV16 or HPV18 E6 and E7 proteins which bound to HLA-A2.1, -A1, -A2.1, -A3.2, -A11.2, and -A24 mols. were identified.

=> s (l12 or l13 or l14 or melief, c?/au) and l11
74 MELIEF, C?/AU
L16 2 (L12 OR L13 OR L14 OR MELIEF, C?/AU) AND L11

=> s l16 not l15
L17 1 L16 NOT L15

=> d an .mh;fil .biotech

L17 ANSWER 1 OF 1 CA COPYRIGHT 1994 ACS
AN 120:189115 CA
TI Human leukocyte antigen-A2.1 restricted candidate cytotoxic T lymphocyte epitopes of human papillomavirus type 16 E6 and E7 proteins identified by using the processing-defective human cell line T2
SO J. Immunother. Emphasis Tumor Immunol. (1993), 14(2), 115-20
CODEN: JIEIEZ; ISSN: 1067-5582
AU **Kast, W. Martin**; Brandt, Remco M. P.; Drijfhout, J. W.; **Melief, Cornelis J. M.**
PY 1993
AB Human papillomavirus type 16 (**HPV**-16) is strongly assocd. with **cervical cancer**. **HPV**-16 cytotoxic T lymphocyte (CTL) epitopes may be good candidates for the

development of an antitumor peptide vaccine. A set of 240 overlapping peptides 9 amino acids in length with an 8 amino acid overlap covering the entire sequence of the 2 viral oncogenes E6 and E7 was synthesized and tested for its ability to bind to the most common human leukocyte antigen class I mol. HLA-A2.1. Binding was measured with the human processing defective cell line T2, which expresses high nos. of empty HLA-A2.1 mols. that are unstable at 37.degree.. These empty mols. can be stabilized by exogenously added peptides, and the extent of stabilization, measured by cell surface HLA-A2.1-specific staining, can be taken as a measure of the relative HLA-A2.1 binding affinity. Following this anal., several HLA-A2.1 binding peptides were pinpointed. Preliminary data suggest that at least one of the high-affinity-binding peptides identified is immunogenic even in an in vitro priming protocol, underlining the feasibility of the method described here to identify the immunogenic peptides and potential candidates for CTL peptide-based vaccines.

FILE 'BIOSIS' ENTERED AT 11:07:36 ON 25 AUG 94
COPYRIGHT (C) 1994 BIOSIS(R)

FILE 'MEDLINE' ENTERED AT 11:07:36 ON 25 AUG 94

FILE 'EMBASE' ENTERED AT 11:07:36 ON 25 AUG 94
COPYRIGHT (C) 1994 Elsevier Science B.V. All rights reserved.

=> s kast w?/au;s melief c?/au;s sette a?/au;s sidney j?/au
FILE 'BIOSIS'
L18 72 KAST W?/AU

FILE 'MEDLINE'
L19 52 KAST W?/AU

FILE 'EMBASE'
L20 49 KAST W?/AU

TOTAL FOR ALL FILES
L21 173 KAST W?/AU

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FILE 'BIOSIS'
L22          242 MELIEF C?/AU

FILE 'MEDLINE'
L23          181 MELIEF C?/AU

FILE 'EMBASE'
L24          132 MELIEF C?/AU

TOTAL FOR ALL FILES
L25          555 MELIEF C?/AU


FILE 'BIOSIS'
L26          126 SETTE A?/AU

FILE 'MEDLINE'
L27           88 SETTE A?/AU

FILE 'EMBASE'
L28           81 SETTE A?/AU

TOTAL FOR ALL FILES
L29          295 SETTE A?/AU


FILE 'BIOSIS'
L30           25 SIDNEY J?/AU

FILE 'MEDLINE'
L31           21 SIDNEY J?/AU

FILE 'EMBASE'
L32           20 SIDNEY J?/AU

TOTAL FOR ALL FILES
L33           66 SIDNEY J?/AU

=> s l33 and l29 and l25 and l21
FILE 'BIOSIS'
L34            1 L30 AND L26 AND L22 AND L18

FILE 'MEDLINE'
L35            1 L31 AND L27 AND L23 AND L19

FILE 'EMBASE'
L36            1 L32 AND L28 AND L24 AND L20

TOTAL FOR ALL FILES
L37            3 L33 AND L29 AND L25 AND L21
```

=> dup rem l37
PROCESSING COMPLETED FOR L37
L38 1 DUP REM L37 (2 DUPLICATES REMOVED)

=> d an ti so au ab

L38 ANSWER 1 OF 1 BIOSIS COPYRIGHT 1994 BIOSIS DUPLICATE 1
AN 94:226187 BIOSIS
TI Role of HLA-A motifs in identification of potential CTL epitopes in
human papillomavirus type 16 E6 and E7 proteins.
SO Journal of Immunology 152 (8). 1994. 3904-3912. ISSN: 0022-1767
AU **Kast W M**; Brandt R M P; **Sidney J**; Drijfhout J-W;
Kubo R T; Grey H M; **Melief C J M**; **Sette A**
AB We have measured the binding affinity for five HLA-A alleles: HLA-A1
(A*0101), A2.1 (A*0201), A3 (A*0301), A11 (A*1101), and A24 (A*2401);
of a set of all possible nonamer peptides (n = 240) of human
papillomavirus type 16 E6 and E7 proteins. High affinity binding
peptides were identified for each of the alleles, thus allowing us to
select several candidates for CTL-based vaccines. Moreover, this
unbiased set of peptides allowed an evaluation of the predictive
value of HLA motifs derived either from the analysis of sequencing of
pools of naturally processed peptides or from the binding analysis of
polyalanine nonameric peptides that differed in the amino acids (aa)
present at the anchor positions. Whereas pool sequencing-derived
motifs were present in only 27% of high affinity binders, the more
expanded motif, based on analysis of different aa substitutions at
the anchor positions, was present in 73% of high affinity binders.
Furthermore, it was found that the presence of anchor residues in a
peptide was in itself not sufficient to determine binding to MHC
class I molecules, because the majority of motif-containing peptides
failed to bind to the relevant MHC. Finally, specific HLA motifs were
used to predict peptide binders of 8, 10, and 11 aa in length.

Several high affinity binding peptides were identified for each of the various peptide lengths, indicating a significant size heterogeneity in peptides capable of high affinity binding to HLA-A molecules.

```
=> s (human papilloma virus or hpv(W)(16 or 18))
FILE 'BIOSIS'
       3103687 HUMAN
          4867 PAPILLOMA
        261401 VIRUS
          1164 HUMAN PAPILLOMA VIRUS
                 (HUMAN(W)PAPILLOMA(W)VIRUS)
          3317 HPV
        208318 16
        198097 18
          1079 HPV(W)(16 OR 18)
L39       2127 (HUMAN PAPILLOMA VIRUS OR HPV(W)(16 OR 18))

FILE 'MEDLINE'
       5149034 "HUMAN"
          7614 "PAPILLOMA"
        194010 "VIRUS"
           685 HUMAN PAPILLOMA VIRUS
                 ("HUMAN"(W)"PAPILLOMA"(W)"VIRUS")
          3495 HPV
        145521 16
        144644 18
          1126 HPV(W)(16 OR 18)
L40       1686 (HUMAN PAPILLOMA VIRUS OR HPV(W)(16 OR 18))

FILE 'EMBASE'
       2428681 "HUMAN"
          5667 "PAPILLOMA"
        223003 "VIRUS"
           539 HUMAN PAPILLOMA VIRUS
                 ("HUMAN"(W)"PAPILLOMA"(W)"VIRUS")
          3107 HPV
        140784 16
        138750 18
           983 HPV(W)(16 OR 18)
L41       1450 (HUMAN PAPILLOMA VIRUS OR HPV(W)(16 OR 18))

TOTAL FOR ALL FILES
L42       5263 (HUMAN PAPILLOMA VIRUS OR HPV(W)(16 OR 18))

=> s l42 and (protein(w)("e6 or e7"))
FILE 'BIOSIS'
        644271 PROTEIN
          1022 "E6"
           972 "E7"
           348 "E6 OR E7"
```

```
                ("E6"(1W)"E7")
            1 PROTEIN(W)("E6 OR E7")
L43         0 L39 AND (PROTEIN(W)("E6 OR E7"))

FILE 'MEDLINE'
       508667 PROTEIN
          816 "E6"
          886 "E7"
          328 "E6 OR E7"
                ("E6"(1W)"E7")
            0 PROTEIN(W)("E6 OR E7")
L44         0 L40 AND (PROTEIN(W)("E6 OR E7"))

FILE 'EMBASE'
       432182 PROTEIN
          729 "E6"
          757 "E7"
          294 "E6 OR E7"
                ("E6"(1W)"E7")
            0 PROTEIN(W)("E6 OR E7")
L45         0 L41 AND (PROTEIN(W)("E6 OR E7"))

TOTAL FOR ALL FILES
L46         0 L42 AND (PROTEIN(W)("E6 OR E7"))

=> s l42 and (protein(w)("e6" or "e7"))
FILE 'BIOSIS'
       644271 PROTEIN
         1022 "E6"
          972 "E7"
           23 PROTEIN(W)("E6" OR "E7")
L47        10 L39 AND (PROTEIN(W)("E6" OR "E7"))

FILE 'MEDLINE'
       508667 PROTEIN
          816 "E6"
          886 "E7"
          262 PROTEIN(W)("E6" OR "E7")
L48       170 L40 AND (PROTEIN(W)("E6" OR "E7"))

FILE 'EMBASE'
       432182 PROTEIN
          729 "E6"
          757 "E7"
           16 PROTEIN(W)("E6" OR "E7")
L49         6 L41 AND (PROTEIN(W)("E6" OR "E7"))

TOTAL FOR ALL FILES
L50       186 L42 AND (PROTEIN(W)("E6" OR "E7"))

=> s l50 and (human mhc class i or mhc class or hla?)
FILE 'BIOSIS'
      3103687 HUMAN
```

```
          12158 MHC
          67080 CLASS
         440136 I
             44 HUMAN MHC CLASS I
                  (HUMAN(W)MHC(W)CLASS(W)I)
          12158 MHC
          67080 CLASS
           4551 MHC CLASS
                  (MHC(W)CLASS)
          32219 HLA?
L51           1 L47 AND (HUMAN MHC CLASS I OR MHC CLASS OR HLA?)

FILE 'MEDLINE'
        5149034 "HUMAN"
          15132 "MHC"
          76893 "CLASS"
         594411 "I"
             43 HUMAN MHC CLASS I
                  ("HUMAN"(W)"MHC"(W)"CLASS"(W)"I")
          15132 "MHC"
          76893 "CLASS"
           8329 MHC CLASS
                  ("MHC"(W)"CLASS")
          36288 HLA?
L52           6 L48 AND (HUMAN MHC CLASS I OR MHC CLASS OR HLA?)

FILE 'EMBASE'
        2428681 "HUMAN"
          11278 "MHC"
          58232 "CLASS"
         400489 "I"
             42 HUMAN MHC CLASS I
                  ("HUMAN"(W)"MHC"(W)"CLASS"(W)"I")
          11278 "MHC"
          58232 "CLASS"
           4001 MHC CLASS
                  ("MHC"(W)"CLASS")
          30321 HLA?
L53           1 L49 AND (HUMAN MHC CLASS I OR MHC CLASS OR HLA?)

TOTAL FOR ALL FILES
L54           8 L50 AND (HUMAN MHC CLASS I OR MHC CLASS OR HLA?)

=> dup rem l54
PROCESSING COMPLETED FOR L54
L55           6 DUP REM L54 (2 DUPLICATES REMOVED)

=> d 1-6 an ti so au ab;s l50 and (l21 or l25 or l29 or l33)

L55  ANSWER 1 OF 6  MEDLINE  1994
AN   94194153     MEDLINE
TI   Role of HLA-A motifs in identification of potential CTL
     epitopes in human papillomavirus type 16 E6 and E7
proteins.
```

SO J Immunol, (1994 Apr 15) 152 (8) 3904-12.
Journal code: IFB. ISSN: 0022-1767.
AU Kast WM; Brandt RM; Sidney J; Drijfhout JW; Kubo RT; Grey HM; Melief
CJ; Sette A
AB We have measured the binding affinity for five **HLA**-A alleles: **HLA**-A1 (A*0101), A2.1 (A*0201), A3 (A*0301), A11 (A*1101), and A24 (A*2401); of a set of all possible nonamer peptides (n = 240) of human papillomavirus type 16 E6 and E7 proteins. High affinity binding peptides were identified for each of the alleles, thus allowing us to select several candidates for CTL-based vaccines. Moreover, this unbiased set of peptides allowed an evaluation of the predictive value of **HLA** motifs derived either from the analysis of sequencing of pools of naturally processed peptides or from the binding analysis of polyalanine nonameric peptides that differed in the amino acids (aa) present at the anchor positions. Whereas pool sequencing-derived motifs were present in only 27% of high affinity binders, the more expanded motif, based on analysis of different aa substitutions at the anchor positions, was present in 73% of high affinity binders. Furthermore, it was found that the presence of anchor residues in a peptide was in itself not sufficient to determine binding to **MHC class** I molecules, because the majority of motif-containing peptides failed to bind to the relevant MHC. Finally, specific **HLA** motifs were used to predict peptide binders of 8, 10, and 11 aa in length. Several high affinity binding peptides were identified for each of the various peptide lengths, indicating a significant size heterogeneity in peptides capable of high affinity binding to **HLA**-A molecules.

L55 ANSWER 2 OF 6 BIOSIS COPYRIGHT 1994 BIOSIS DUPLICATE 1
AN 94:160183 BIOSIS
TI Limitations of predictive motifs revealed by cytotoxic T lymphocyte epitope mapping of the **human papilloma virus** E7 protein.
SO International Immunology 6 (2). 1994. 289-296. ISSN: 0953-8178

AU Sadovnikova E; Zhu X; Collins S M; Zhou J; Vousden K; Crawford L;
Beverley P; Stauss H J
AB **Human papilloma virus** (HPV) type 16 is found in the majority of cervical cancer patients and the transforming **protein E7** is consistently expressed in cancer cells, making it a potential target for immune attack. In this study we have investigated whether E7 gains access to the **MHC class** I processing pathway and provides cytotoxic T lymphocyte (CTL) stimulating peptide epitopes. CTL were induced in H-2-b mice by immunization with recombinant vaccinia virus expressing E7 (Vac-E7). To map CTL recognition, natural peptides were purified from cells expressing either Intact or truncated E7 protein. Following peptide separation by HPLC one major CTL epitope was detected and truncated constructs localized this epitope to the C-terminal region. Mapping with synthetic peptides indicated that residues 49 - 57 (RAHYNIVTF) were recognised by anti-E7 CTL. Synthetic 49 - 57 peptide was used to induce CTL, which recognized the same HPLC purified natural peptide fractions as anti-E7 CTL. Binding motifs for H-2-b class I molecules did not predict residues 49 - 57 to be a CTL epitope, but instead the sequence 21 - 28 (DLYCYEQL) which contains a Kb anchor motif. Synthetic 21 -28 peptide was found to bind to K-b Class I molecules and readily induced CTL, indicating that the T cell repertoire of H-2-b mice can recognize this epitope. However, these CTL did not recognize peptides isolated from E7 expressing cells, showing that natural processing did not produce detectable levels of the 21 - 28 epitope. Together, the data demonstrate that an unexpected E7 peptide can function as a major CTL epitope.

L55 ANSWER 3 OF 6 MEDLINE 1994
AN 94020819 MEDLINE
TI **MHC class** I expression in **HPV 16** positive cervical carcinomas is post-transcriptionally

controlled and independent from c-myc overexpression.
SO Oncogene, (1993 Nov) 8 (11) 2969-75.
Journal code: ONC. ISSN: 0950-9232.
AU Cromme FV; Snijders PJ; van den Brule AJ; Kenemans P; Meijer CJ;
Walboomers JM
AB Squamous cell carcinomas of the uterine cervix (n = 23) were selected for the presence of human papillomavirus type 16 (**HPV 16**) using the polymerase chain reaction (PCR).
Localization of transcripts coding for the E7 protein was demonstrated in neoplastic cells with RNA in situ hybridization.
Consecutive tissue sections were investigated for expression of the
major histocompatibility complex class I (MHC-I) and c-myc using
immunohistochemical double staining procedures, since a role has
been suggested for the c-myc protein in MHC-I down-regulation and
c-myc overexpression has been described in cervical carcinomas.
Reduced expression of class I heavy chains was observed in
neoplastic cells from 18 out of 23 carcinomas (78%). Varying levels
of c-myc overexpression were observed in 12 carcinomas (52%), from
which four showed positive MHC-I expression in c-myc overexpressing
cells. In the remaining eight c-myc overexpressing carcinomas MHC-I
down-regulation was observed. Additional RNA in situ hybridization
with class I heavy chain locus-specific RNA-probes revealed presence
of class I mRNAs in those neoplastic cells that show negative
staining for MHC-I protein. These data strongly indicate that MHC-I
down-regulation in cervical carcinomas involves post-transcriptional
mechanisms, not directly related to E7 transcription and overexpression of c-myc.

L55 ANSWER 4 OF 6 MEDLINE 1994
AN 93380495 MEDLINE
TI Vaccination with cytotoxic T lymphocyte epitope-containing peptide
protects against a tumor induced by human papillomavirus type
16-transformed cells.
SO Eur J Immunol, (1993 Sep) 23 (9) 2242-9.
Journal code: EN5. ISSN: 0014-2980.

AU Feltkamp MC; Smits HL; Vierboom MP; Minnaar RP; de Jongh BM; Drijfhout JW; ter Schegget J; Melief CJ; Kast WM
AB Cytotoxic T lymphocyte (CTL) peptide epitopes can be used for immunization of mice against lethal virus infection. To study whether this approach can be successful against virus-induced tumors we generated a B6 (H-2b) tumorigenic cell line transformed by human papillomavirus (HPV). This virus is detected in over 90% of all human cervical cancers. To identify vaccine candidates, we generated a set of 240 overlapping peptides derived from the HPV type 16 (HPV16) oncogenes E6 and E7. These peptides were tested for their ability to bind H-2Kb and H-2Db **MHC class** I molecules. Binding peptides were compared with the presently known peptide-binding motifs for H-2Kb and H-2Db and the predictive value of these motifs is shortly discussed. The high-affinity H-2Db-binding peptide and putative CTL epitope E7 49-57 (RAHYNIVTF) was used in vaccination studies against **HPV 16** -transformed tumor cells. Immunization with peptide E7 49-57 rendered mice insensitive to a subsequent challenge with **HPV 16**-transformed tumor cells in vivo, and induced a CTL response which lysed the tumor cells in vitro.

L55 ANSWER 5 OF 6 MEDLINE 1994
AN 93247581 MEDLINE
TI [In vivo identification of YB-1 protein, interacting with the enhancer of human papillomavirus (HPV) type 18, using antibodies to a synthetic peptide].
Identifikatsiia in vivo belka YB-1, vzaimodeistvuiushchego s enkhancerom virusa papilloma cheloveka (HPV) tipa 18 s pomoshch'iu antitel k sinteticheskomu peptidu.
SO Mol Biol (Mosk), (1993 Jan-Feb) 27 (1) 81-91.
Journal code: NGX. ISSN: 0026-8984.
AU Spitkovskii DD; Roier GD; Mazurenko NN; Mikhaleva II; Prudchenko IA; Korbukh IA; Sukhova NM; Kiselev FL
AB Enhancer sequences of **human papilloma virus** (HPV) type 18 were used for screening of HeLa cells cDNA library in lambda gt11 using the protein binding method. Clones with YB I gene homology sequences were isolated. This gene is coding

the protein which binds the regulatory region of Y gene of main histocompatibility complex (**HLA** 11). The YB I transcripts were revealed in all tested samples of cervical carcinomas. To analyze the protein the rabbit antibodies were produced to synthetic peptide, which corresponds to the most hydrophilic region of the protein. This antipeptide serum allowed to identify the nuclear 42K protein in HeLa cells as well as in normal fibroblasts.

L55 ANSWER 6 OF 6 MEDLINE 1994
AN 92097117 MEDLINE
TI Leukoregulin and gamma-interferon inhibit human papillomavirus type 16 gene transcription in human papillomavirus-immortalized human cervical cells.
SO Cancer Res, (1992 Jan 15) 52 (2) 456-63.
Journal code: CNF. ISSN: 0008-5472.
AU Woodworth CD; Lichti U; Simpson S; Evans CH; DiPaolo JA
AB The human papillomavirus (HPV) transforming genes E6 and E7 are retained and expressed in the majority of cervical cancers implying an important role for these proteins in maintenance of the malignant phenotype. Leukoregulin (LR) and recombinant gamma-interferon (r-IFN-gamma), lymphokines secreted by immune cells present in regressing HPV infections, inhibited transcription of E6/E7 RNAs in several human cervical epithelial cell lines immortalized by recombinant **HPV-16**, -18, and -33 DNAs. r-IFN alpha was not effective. Reduction in E6/E7 RNA expression was accompanied by inhibition of cell proliferation coincident with an increase in epidermal transglutaminase activity, a marker of squamous differentiation. LR and r-IFN gamma enhanced transcription of class 1 cell surface histocompatibility antigens (**HLA**) and r-IFN gamma additionally induced **HLA** class 2 expression. HPV-immortalized cells developed partial resistance to the growth inhibitory effects of lymphokines after malignant transformation or extended propagation in culture. This is the first demonstration that LR and r-IFN gamma selectively inhibit transcription of HPV-transforming genes and suggests a molecular

mechanism by which these lymphokines participate in regression of
premalignant cells.

FILE 'BIOSIS'
L56 0 L47 AND (L18 OR L22 OR L26 OR L30)

FILE 'MEDLINE'
L57 2 L48 AND (L19 OR L23 OR L27 OR L31)

FILE 'EMBASE'
L58 0 L49 AND (L20 OR L24 OR L28 OR L32)

TOTAL FOR ALL FILES
L59 2 L50 AND (L21 OR L25 OR L29 OR L33)

=> d 1-2

L59 ANSWER 1 OF 2 MEDLINE 1994
AN 94194153 MEDLINE
TI Role of HLA-A motifs in identification of potential CTL epitopes in
human papillomavirus type 16 E6 and E7 proteins.
AU **Kast WM**; Brandt RM; **Sidney J**; Drijfhout JW; Kubo RT; Grey HM; **Melief CJ**; **Sette A**
CS Department of Immunohematology, University Hospital Leiden, The
Netherlands.
NC 1RO1 CA 57933-01 (NCI)
AI18634 (NIAID)
SO J Immunol, (1994 Apr 15) 152 (8) 3904-12.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 9407

L59 ANSWER 2 OF 2 MEDLINE 1994
AN 93380495 MEDLINE
TI Vaccination with cytotoxic T lymphocyte epitope-containing peptide
protects against a tumor induced by human papillomavirus type
16-transformed cells.
AU Feltkamp MC; Smits HL; Vierboom MP; Minnaar RP; de Jongh BM; Drijfhout JW; ter Schegget J; **Melief CJ**; **Kast WM**
CS Department of Immunohematology and Blood bank, University Hospital
Leiden, The Netherlands.
SO Eur J Immunol, (1993 Sep) 23 (9) 2242-9.

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     Journal code: EN5. ISSN: 0014-2980.
CY   GERMANY: Germany, Federal Republic of
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals; Cancer Journals
EM   9312

=> s hpv and cervical(w)(carcinoma or cancer or adenoma)
FILE 'BIOSIS'
          3317 HPV
         49743 CERVICAL
        148553 CARCINOMA
        198689 CANCER
         15544 ADENOMA
         13451 CERVICAL(W)(CARCINOMA OR CANCER OR ADENOMA)
L60        655 HPV AND CERVICAL(W)(CARCINOMA OR CANCER OR
ADENOMA)

FILE 'MEDLINE'
          3495 HPV
         51003 CERVICAL
        193345 CARCINOMA
        187135 CANCER
         31527 ADENOMA
          6551 CERVICAL(W)(CARCINOMA OR CANCER OR ADENOMA)
L61        603 HPV AND CERVICAL(W)(CARCINOMA OR CANCER OR
ADENOMA)

FILE 'EMBASE'
          3107 HPV
         44499 CERVICAL
        181363 CARCINOMA
        343117 CANCER
         17655 ADENOMA
          5370 CERVICAL(W)(CARCINOMA OR CANCER OR ADENOMA)
L62        497 HPV AND CERVICAL(W)(CARCINOMA OR CANCER OR
ADENOMA)

TOTAL FOR ALL FILES
L63       1755 HPV AND CERVICAL(W)(CARCINOMA OR CANCER OR
ADENOMA)

=> s l63 and (l21 or l25 or l29 or l33)
FILE 'BIOSIS'
L64          0 L60 AND (L18 OR L22 OR L26 OR L30)

FILE 'MEDLINE'
L65          1 L61 AND (L19 OR L23 OR L27 OR L31)

FILE 'EMBASE'
L66          1 L62 AND (L20 OR L24 OR L28 OR L32)

TOTAL FOR ALL FILES
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```
L67          2 L63 AND (L21 OR L25 OR L29 OR L33)

=> dup rem l67
PROCESSING COMPLETED FOR L67
L68           1 DUP REM L67 (1 DUPLICATE REMOVED)

=> d

L68  ANSWER 1 OF 1  MEDLINE  1994
DUPLICATE 1
AN   94107849     MEDLINE
TI   Human leukocyte antigen-A2.1 restricted candidate cytotoxic
T
     lymphocyte epitopes of human papillomavirus type 16 E6 and
E7
     proteins identified by using the processing-defective human
cell
     line T2.
AU   Kast WM; Brandt RM; Drijfhout JW; Melief CJ
CS   Department of Immunohematology, University Hospital,
Leiden, The
     Netherlands.
NC   1RO1 CA57933-01 (NCI)
SO   J Immunother, (1993 Aug) 14 (2) 115-20.
     Journal code: AZ0. ISSN: 1053-8550.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   9404

=> s (hpv and allele and hla(w)(a11 or a1 or a2 or a3))
FILE 'BIOSIS'
          3317 HPV
         18714 ALLELE
         32038 HLA
           384 A11
          9564 A1
         16266 A2
          3233 A3
          1363 HLA(W)(A11 OR A1 OR A2 OR A3)
L69          0 (HPV AND ALLELE AND HLA(W)(A11 OR A1 OR A2 OR A3))

FILE 'MEDLINE'
          3495 HPV
         11879 ALLELE
         34933 HLA
           361 A11
          8641 A1
         18625 A2
          3380 A3
          1538 HLA(W)(A11 OR A1 OR A2 OR A3)
L70          0 (HPV AND ALLELE AND HLA(W)(A11 OR A1 OR A2 OR A3))
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FILE 'EMBASE'
          3107 HPV
         13053 ALLELE
         30156 HLA
           308 A11
         12128 A1
         20375 A2
          2584 A3
          1380 HLA(W)(A11 OR A1 OR A2 OR A3)
L71          1 (HPV AND ALLELE AND HLA(W)(A11 OR A1 OR A2 OR A3))

TOTAL FOR ALL FILES
L72          1 (HPV AND ALLELE AND HLA(W)(A11 OR A1 OR A2 OR
A3))

=> d

L72  ANSWER 1 OF 1  COPYRIGHT 1994 ELSEVIER SCI. B.V.
AN   94218259  EMBASE
TI   Isolation and characterization of tumor-infiltrating
lymphocytes
     from cervical carcinoma.
AU   Hilders C.G.J.M.; Ras L.; Van Eendenburg J.D.H.; Nooyen Y.;
Fleuren
     G.J.
CS   Department of Pathology, University of Leiden, P.O. Box
9603, 2300
     RC Leiden, Netherlands
SO   INT. J. CANCER, (1994) 57/6 (805-813).
     ISSN: 0020-7136  CODEN: IJCNAW
CY   United States
DT   Journal
FS   010     Obstetrics and Gynecology
     016     Cancer
     026     Immunology, Serology and Transplantation
LA   English
SL   English

=> fil reg
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